E.M.

UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark ffice

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SERIAL NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.

12M1/0603

LEGAL AFFAIRS DEPARTMENT
CELL THERAPEUTICS INC
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SEATTLE WA 98119

EXAMINER	
ART UNIT	**PAPER NUMBER**

DATE MAILED:

Below is a communication from the EXAMINER in charge of this application

COMMISSIONER OF PATENTS AND TRADEMARKS

ADVISORY ACTION

☐ THE PERIOD FOR RESPONSE:

☐ is extended to run _____ from the date of the Final Rejection

☐ continues to run _____ from the date of the Final Rejection

☐ expires three months from the date of the final rejection or as of the mailing date of this Advisory Action, whichever is later. In no event however, will the statutory period for response expire later than six months from the date of the final rejection.

Any extension of time must be obtained by filing a petition under 37 CFR 1.136(a), the proposed response and the appropriate fee. The date on which the response, the petition, and the fee have been filed is the date of the response and also the date for the purposes of determining the period of extension and the corresponding amount of the fee. Any extension fee pursuant to 37 CFR 1.17 will be calculated from the date that the shortened statutory period for response expires as set forth above.

☒ Appellant's Brief is due in accordance with 37 CFR 1.192(a).

☒ Applicant's response to the final rejection, filed 4/18/97. has been considered with the following affect, but it is not deemed to place the application in condition for allowance:.

1. ☒ The proposed amendments to the claim and/or specification will not be entered and the final rejection stands because:

   a. ☐ There is no convincing showing under 37 CFR 1.116(b) why the proposed amendment is necessary and was not earlier presented.

   b. ☒ They raise new issues that would require further consideration and/or search. (See Note).

   c. ☒ They raise the issue of new matter. (See Note).

   d. ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal.

   e. ☐ They present additional claims without cancelling a corresponding number of finally rejected claims

   NOTE: _____

2. ☐ Newly proposed or amended claims _____ would be allowed if submitted in a separately filed amendment cancelling the non-allowable claims.

3. ☐ Upon the filing of an appeal, the proposed amendment ☐ will be ☐ will not be, entered and the status of the claims in this application would be as follows:

   Allowed claims: _____
   Claims objected to: _____
   Claims rejected: _____
   However;

   a. ☐ The rejection of claims _____ on references is deemed to be overcome by applicant's response.
   b. ☐ The rejection of claims _____ on non-reference grounds only is deemed to be overcome by applicant's response.

4. ☐ The affidavit, exhibit or request for reconsideration has been considered but does not overcome the rejection.

5. ☐ The affidavit or exhibit will not be considered because applicant has not shown good and sufficient reasons why it was not earlier presented.

☐ The proposed drawing correction ☐ has ☐ has not been approved by the examiner.

☐ Other

The amendment introduces new issues and new matter:

1. R_5= Me_2N is clearly new matter.

a. Such a choice would permit far more than the Me_2N CO of the claim 14 species. It would also permit $X(R_5)m$= e.g. $C(NMe)_3$, or $C(OH)(NMe)_2$, etc.

b. Even $X(R_5)m$= $CO(NMe_2)$ is described only for that one species, with that specific choice of R_2 and R_3, etc., not all others. Thus, such a $CO(NMe_2)$ species for R_2=OH is not described or embraced by any genus.

2. The proviso limiting R_5=H to two lacks description. Even negative limitations require description (Ex parte Grasselli, 231 USPQ 393).

3. Some of the new substituents are undefined. For example, "sulfonato" is presumably RSO_2O; but what is R? Similarly, phosphono, etc. The original stems required alkyl but the new terms are broader.

3. What is "phospho". This is a prefix denoting the presence of the element P.

4. What is thioalkoxy? Is this mercaptoalkoxy? Alkylthio?

5. Applicants have replaced two claim 12 forms with 2 others, but there is no evidence that one skilled in the art would know that the new term was truly

intended. In fact "benzamino" would be understood as something bound via a nitrogen. But aminophenyl is bound by the phenyl ring and is not a likely choice.

6. In other places, applicants have made arbitrary choices as to placement of substituents, eg. Claim 10.

7. The replacement of carboxy alkyl with CO_2H replaces one problem with another. The original term was "carboxylic acid," i.e. RCO_2H, which has no valency. The new term $-CO_2H$ is clearly different and is an arbitrary choice (as $-R-CO_2H$ and even -OC(O)R would have been alternatives).

There may be other problems as well.

Applicant's argument on point 10 is unpersuasive. The term does not exist in the specification and thus does not find description there. It is a subsequent generalization of the moiety that occurs in 45 & 47R and hence is broader than the actual choice there, even assuming that such species falls within the genus.

Point 6 is withdrawn; page 5, lines 9-10 indicate lisofylline is only a preferred choice.

The argument on point 20 is unpersuasive. "Carbocyclic Group" simply means any group containing a carbocycle anywhere. Thus, R_5 is in effect, -X-A,

where A is a carbocycle with certain permitted substituents, but -X- is an undefined linking group.

The argument about dosage is unpersuasive. The examiner is not requiring clinical data. But, as set forth in Gardner, a dosage range too large, e.g. 10,000 fold is not enabling. Applicant refers to lisofylline as "a drug which has been the subject of clinical investigation". However,

a. The claims are far broader than lisofylline prodrugs, as other choices are permitted for e.g. R_2 and n.

b. Effective dosage for lisofylline, desc~~ription~~s "clinical investigation" has not yet been determined. This is evidence that contradicts applicants assertion that there is "a very high skill level in the art." If all this "clinical investigation" has still not found the proper dosage for this one compound, how much more so it will for a genus of millions.

The argument on point 2 is likewise unpersuasive. An impasse has been reached because applicants and examiner are clearly reading the specification differently. Page 4, lines 8-11 clearly state that these compounds are to be hydrolyzed to the corresponding alcohol. But the body is incapable of hydrolyzing

those ethers, and hence they cannot meet the basic requirement. Applicant suggests this arises "in the context of a synthetic method, not exclusively in the context of a therapeutic application" but there is no evidence for this. While it is agreed that "prophetic examples do not make the disclosure non-enabling", where a significant category of compounds has been shown inoperative, applicants must either rebut the reasoning or narrow the claims accordingly. (In re Cook, 169 USPQ 798, 302; In re Corkill, 226 USPQ 1005, 1009).

Applicants arguments on the hydrolysis to lisofylline argument (point 3) is largely unpersuasive. It is agreed that lisofylline is only preferred, and that other analogs are also covered. However, for reasons set forth in point b above, even compounds which hydrolyze to lysofylline are not enabling. This is a point under 35 USC 112, not 35 USC 101. There is no 35 USC 101 rejection in the Final Rejection.

A facsimile center has been established in Group 1200, room 3C10. The hours of operation are Monday through Friday, 8:45 AM to 4:45 PM. The telecopier numbers for accessing the facsimile machine are (703) 308-4556 or (703) 305-3592.

Any inquiry concerning this communication should be directed to Examiner Berch at telephone number (703) 308-4718.

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BERCH; aco

June 2, 1997